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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,833	11/21/2003	David Epstein	23239-541 (ARC-41)	3645

30623 7590 01/06/2006

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EXAMINER

ASHEN, JON BENJAMIN

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 01/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/718,833	Applicant(s) EPSTEIN ET AL.	
	Examiner Jon B. Ashen	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11/21/03 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>11/04; 11/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-10 and PDGF as the target protein of the claimed aptamer composition, in the reply filed on 10/06/05 is acknowledged.

Status of the Application

2. Claims 1-8 and 10 are pending in this application. Claims 9 and 11-57 were cancelled by Applicant in the communication filed 10/06/05. Claims 1-8 and 10 are currently under examination.

Specification

3. The use of the trademark SELEXTM has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied

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with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Provisional Application No. 60,428,102 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application because no disclosure of PDGF aptamers could be found. Additionally, Provisional Application No. 60,469,628 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application because no disclosure of PDGF aptamers linked by a non-nucleotide linker could be found.

Therefore, the effective filing date of claims 1-7, drawn to aptamers that are not required to be PDGF aptamers is considered to be 11/21/02, the filing date of Provisional Application No. 60,428,102 and the effective filing date of claim 8, drawn to PDGF aptamers that are required to be linked by non-nucleotide linkers is considered to be 11/21/2003. If Applicant believes that adequate support is provided by the

disclosures of either prior filed application, Applicant is invited to point, with particularity, to where such support may be found.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-4, 6-8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the relationship between the nucleic acid (a) and the stabilizing moiety that comprises a linking moiety (b). The claim as set forth does not require that the stabilizing moiety that comprises a linking moiety either stabilize or link the nucleic acid that comprises two or more aptamers in the claimed composition and the skilled artisan cannot determine the metes and bounds of what is being claimed, without assumption, because they cannot determine what is to be stabilized or linked. It cannot be determined if the claimed nucleic acid that comprises two or more aptamers is only required to be present in the composition with the claimed stabilizing moiety that comprises a linking moiety, for example or if the two or more aptamers comprised by the nucleic acid are linked by the linking moiety, for example, or if something else in the claimed composition is to be linked by the linking moiety, for example. Claims 2-3, 6-7, 8 and 10 are rejected due to their dependence on an indefinite claim.

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7. Claims 1-4, 6-8 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites, "a nucleic acid comprising one or more aptamers." However, the skilled artisan cannot determine the metes and bounds of what is being claimed with this terminology, without assumption, for the following reasons. Aptamer is not defined in the claim and the disclosure of the specification indicates that aptamers are nucleic acid molecules having specific binding affinities (pg. 1). As set forth, claim 1 is drawn to "a nucleic acid" indicating a single nucleic acid molecule. As described in the specification, "Aptamers are nucleic acid molecules (pg. 3, [0003])," indicating that aptamers are also single nucleic acid molecules. Additionally, claim 4 is drawn to a nucleic acid that comprises first and second aptamers, the metes and bounds of which cannot be determined for the reasons set forth above. Therefore, it is not clear how a nucleic acid can comprise two or more aptamers, which appear to be discrete nucleic acid molecules in and of themselves. Claims 2-3, 6-7, 8 and 10 are rejected due to their dependence on an indefinite claim.

8. Claims 1-4 and 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "high molecular weight" in claim 1 is a relative term which renders the claim indefinite. The term "high molecular weight" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably

apprised of the scope of the invention. Claims 2-4 and 6-8 are rejected due to their dependence on an indefinite claim.

9. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 recites, "The aptamer composition of claim 1, wherein the high molecular weight aptamer composition has a molecular weight selected from the group of molecular weights as listed. However, the skilled artisan cannot determine the metes and bounds of what is being claimed with this terminology, without assumption, for the following reasons. The molecular weight of a composition is the sum total weight of all molecules comprised within the composition. The scope of the molecular weight of the claimed composition, therefore, cannot be determined from the claim language because there are no volumes or quantities claimed. Without particular knowledge of the volumes or quantities comprised in the claimed composition, the molecular weight of the composition cannot be determined without assumption.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

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1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-7 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 13 and 37 of copending Application No. 10/762,915. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The claims of the instant application embrace a broad genus of aptamer compositions comprising two or more aptamers and a stabilizing moiety comprising a linking moiety wherein the linking moiety is not a nucleic acid, a specific embodiment of which is claimed as a pharmaceutical composition in claims 1, 13 and 37 of - 8 of copending Application No. 10/762,915. MPEP § 2131.02 states that "A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus." The species in that case will anticipate the genus. In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989).

Therefore, one of ordinary skill in the art would have found it obvious to make the instantly claimed aptamer composition comprising two or more aptamers and a stabilizing moiety comprising a linking moiety wherein the linking moiety is not a nucleic

acid because a specific embodiment which is embraced within this genus, that is a pharmaceutical composition comprising two or more aptamers linked together in a linear arrangement by PEG, as instantly claimed, is claimed in copending Application No. 10/762,915.

This is a provisional obviousness-type double patenting rejection.

12. Claims 1-8 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-17 and 36 of copending Application No. 10/873,853. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The claims of the instant application embrace a broad genus of aptamer compositions capable of binding PDGF comprising two or more aptamers and a stabilizing moiety comprising a linking moiety wherein the linking moiety is not a nucleic acid wherein the linking moiety is PEG and the composition has a molecular weight as specified in claim 10 wherein the composition has a structure that comprises a first aptamer – PEG – a second aptamer linear structure, a specific embodiment of which is claimed as the aptamer composition of claims 10-17 and 36 of copending Application No. 10/873,853 which are drawn to compositions of aptamers comprising two or more aptamers linked together in linear arrangements aptamer-PEG-aptamer-PEG-aptamer, for example, wherein the PEG is identified (see claim 17 for example) as 20kD or 30kD PEG, for example. MPEP § 2131.02 states that “A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus.” The

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species in that case will anticipate the genus. In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989).

Therefore, one of ordinary skill in the art would have found it obvious to make the instantly claimed aptamer composition comprising two or more aptamers and a stabilizing moiety comprising a linking moiety wherein the linking moiety is not a nucleic acid, as above, because claims 10-17 and 36 of copending Application No. 10/873,853 disclose a specific embodiment which is embraced within this genus, that is an aptamer composition comprising a linear arrangement of first and second aptamers that are capable of binding to PDGF wherein the aptamers are linked by non-nucleotide linkers that are PEG moieties.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Janjic et al. (US 6,229,002). The instant invention set forth in claims 1-8 and 10 is drawn to a high molecular weight aptamer composition comprising a nucleic acid comprising two or more aptamers, and a stabilizing moiety comprising a linking moiety

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wherein the linking moiety is not a nucleic acid wherein the linking moiety comprises a polyalkylene glycol that is a polyethylene glycol (PEG), wherein the composition has a linear arrangement comprising the structure (aptamer-PEG-aptamer) wherein the PEG is multi or bi activated, the aptamer is capable of binding to PDGF and the molecular weight of the composition is selected from the group consisting of greater than 10kD, 20Kd, 40Kd and 80Kd.

Janjic et al. disclose PDGF nucleic acid ligands covalently linked to non-immunogenic high molecular weight compounds that are polyethylene glycol (PEG) polymers that have a molecular weight of 10-80Kd (col. 10, lines 1-36). Janjic et al. disclose that in certain embodiments, the PDGF ligands of their invention can be represented as Y-B'-Y'-B''-Y'' wherein Y, Y' and Y'' are segments of different PDGF nucleic acid ligands and B' and/or B'' are spacers or linker molecules (col. 14, lines 45-54) and that linkers, which are also known as spacers, can be PEG (col. 16, lines 39-48), which is considered a disclosure that anticipates the linear arrangement of the instant composition as set forth in claim 4. Based on the 112 2nd paragraph rejection above, the disclosure of Janjic et al. is reasonably considered to be a disclosure of an embodiment that falls within the scope of what is claimed. Janjic et al. disclose that in embodiments where the non-immunogenic high molecular weight compound is polyalkylene or polyethylene glycol, the aptamer is preferably bonded to the PEG by the 5' or 3' hydroxyl thereof (col. 18, lines 50-61). Janjic et al. disclose that in certain embodiments, a plurality of aptamers can be associated with a single PEG wherein the plurality of aptamers are targeted to PDGF or to PDGF and a different target (col. 26,

line 62-col. 27, line 14). The disclosure of a plurality of aptamers targeted to PDGF that are associated with a single PEG moiety is reasonably considered a disclosure of a composition comprising two or more aptamers and PEG wherein the PEG is bi and multiactivated PEG, because the disclosure of a single PEG that is covalently bound to at least two aptamers indicates that the PEG was at least "bi-activated" in accordance with the instant invention (see disclosure of the specification at pg. 10 [0043]) such that it would form 2 covalent bonds with the 3' OH and 5' OH of different aptamers.

Therefore, the instant invention as set forth in claims 1-8 and 10 is anticipated by Janjic et al. (US 6,229,002).

15. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Gold et al. (WO 00/04184). The invention set forth in claims 1-7 is relied upon as above.

Gold et al. disclose bivalent binding molecules that comprise first and second binding domains that are aptamers to first and second epitopes of 7TM G protein coupled receptors that are coupled to each other via either their 5' or 3' ends via a linker wherein the linker can be a polynucleotide or polyethylene glycol (pg. 6, line 32 to pg. 7, line 10; pg. 9, lines 1-4 and 26-34; pg. 21). Based on the 112 2nd paragraph rejection above, the disclosure of Gold et al. is reasonably considered to be a disclosure of an embodiment that falls within the scope of what is claimed. The disclosure of Gold et al. on pg. 21, states "the first and second binding domains are covalently coupled via a linker," and is reasonably interpreted as a disclosure of a nucleic acid comprising 2 aptamers that are joined in a linear arrangement wherein the first aptamer is linked to a

first terminus of the PEG linking moiety and wherein the second aptamer is linked to a second terminus of the PEG linking moiety. Additionally, disclosures above, of first and second aptamers covalently coupled to a linker wherein the linker can be PEG, is reasonably considered an inherent disclosure of the instant composition that comprises two or more aptamers and bi-activated PEG (which also reads on multi-activated PEG) because if the PEG were not bi-activated, it could not be covalently bound to both the first and second aptamers. Moreover, Gold et al. disclose stabilizing moieties that can be added to nucleic acid aptamers that are modified chemical groups that include 2' position sugar modifications (pg. 22, beginning line 16). This disclosure of Gold et al., in combination with the disclosure of polynucleotide linkers above, is reasonably considered, based on the 112 2nd paragraph rejection above, a disclosure that anticipates an embodiment of the instant invention that falls within the scope of claim 1, that is a high molecular weight aptamer composition comprising a nucleic acid that is a single nucleic acid molecule comprising two or more aptamers, and a stabilizing moiety comprising a linking moiety wherein the linking moiety is not a nucleic acid because it is the bond between the 2'F sugar modification (2' F modifications disclosed on pg. 23) and the ribose sugar.

Therefore, Gold et al. (WO 00/04184) anticipate the instant invention as set forth in claims 1-7.

16. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Lannigan et al. (WO 00/11446). The invention as set forth in claims 1-7 is relied upon as above.

Lannigan et al. disclose oligonucleotide based biosensors that are a combination of two or more different aptamers linked together by a polymeric linker (termed "biaptamers") that have a structure comprising A-L-B wherein A and B are aptamers and L is a linker (Abstract; pg. 4, lines 23-29; pg. 5, lines 21-32). Lannigan et al. disclose that the structure A-L-B can be comprised in the structure F1-A-L-B-F2 wherein F1 and F2 are fluorescent molecules. This disclosure is reasonably interpreted, based on the 112 2nd paragraph rejection above, as a disclosure of an embodiment of the instant invention that falls within the scope of claim 1, that is a high molecular weight aptamer composition comprising a nucleic acid comprising two or more aptamers and a stabilizing moiety comprising a linking moiety wherein the linking moiety is not a nucleic acid because it is the bond between the F1 or F2 stabilizing moieties and the A and B aptamers. Lannigan et al. disclose that two aptamers that show mutually independent binding to a specific target are linked together to form a "biaptamer" thru a linker (L) moiety that can be either a nucleic acid or polyethylene glycol (PEG) (pg. 8, lines 11-28) and that multiple aptamers can be linked to the polymer backbone of the linker to form a "polyaptamer." The disclosure which is reasonably considered to be a disclosure of bi and multiactivated linker that is a bi or multiactivated PEG.

Therefore, Lannigan et al. (WO 00/11446) anticipate the instant invention as set forth in claims 1-7.

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Cubicciotti (US 6,287,765).
2. Janjic et al. (US 6,329,145).

Conclusion

18. No claims are allowed.
19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jba

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